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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/965,201 | 09/25/2001 | Steven J. Brown | AXIOM.016A | 2903 |

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David B. Waller & Associates
5677 Oberlin Drive
Suit 214
San Diego, CA 92121

| EXAMINER | |
|---|---|
| GARVEY, TARA L | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | |

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/965,201 | BROWN ET AL. | |
| | Examiner | Art Unit | |
| | Tara L Garvey | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *July 26, 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10, 12-25 and 41-42* is/are rejected.

7)☒ Claim(s) *11 and 26-40* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/4/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *PTO-413B*.

## DETAILED ACTION

Claims 1-42 are pending. Claims 43-52 were cancelled in an election to a restriction requirement filed on July 26, 2004.

### *Election/Restrictions*

Applicant's election without traverse of Group I in the reply filed on July 26, 2004 is acknowledged.

Claims 43-52 were cancelled. Claim 8 was withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on July 26, 2004.

### *Claim Objections*

Claims 11 and 26-40 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title; if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10/1/04

Claims 1-10, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lorens et al (US 2004/0002056 of which the effective date is May 10, 2001) in view of Case et al and further in view of Grissmer et al.

Lorens et al teaches a method of screening bioactive agents by expressing an inducible promoter linked to a gene of interest in a cell, inducing the promoter, adding candidate bioactive agent and screening for an altered phenotype. The also teach that the inducible promoter can be a tetracycline regulated promoter and that the altered phenotype can be a physiological change in the cell such as membrane potential or ion flux (page 2, left column, third and sixth paragraphs; page 4, right column, last paragraph, lines 1-4; page 5, left column, third full paragraph; page 6, left column, first full paragraph, page 49, claims 1, 14 and 15).

Lorens does not teach repeating the contacting step with additional compounds. Case et al teaches that after the initial compound that addition compounds can be tested in a screening assay (column 45, lines 62-66).

Lorens et al do not teach potassium ion channels. Grissmer et al teaches a stable cell line that expresses potassium ion channels that are used to screen drugs that modulate the potassium ion channels.

It would have been obvious to modify the teachings of Lorens et al to screen multiple compounds that modulate potassium ion channels during one experiment because Lorens et al teach the contacting of a compound with a cell followed by the measurement of a physiological change such as membrane potential or ion flux and because Case et al and Grissmer et al teach that potassium ion channels can be used in a drug screening method and that the screening can be repeated. One would have been motivated to do so in order to receive the expected benefit, as suggested by Lorens et al and exemplified by Case et al and Grissmer et al, of using a drug screening system for identifying drugs that modulate the activity of a potassium ion channel multiple times once the expression of the potassium ion channel has been induced. Absent of any evidence to the contrary, there would have been a reasonable expectation of success in screening multiple drugs once the expression of the potassium ion channel was induced since the system was already known to be functional from the first compound.

Claims 14-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uchino et al (Molecular Brain Research, 1997, volume 44, pages 1-11) in view of Renard et al (European Journal of Pharmacology, 1999, volume 366, pages 319-328) and in further view of Grissmer et al (Molecular Pharmacology, 1994, volume 45, pages 1227-1234).

Uchino et al teach a drug screening assay in which the NMDA receptor is expressed in CHO cells under the control of the inducible hsp70 promoter, the levels of the current were measured, antagonists were added to the system and the Ca2+ levels were measured in response to the compounds added (abstract; page 2, left column, second paragraph; page 4, right column, third paragraph bridging page 6, left column; page 7, left column, second paragraph bridging page 8, right column). The NMDA receptor reads on an ion channel target and the measurement of the Ca2+ levels will determine if the molecule has modulated the ion channel target.

Uchino et al do not teach the tetracycline inducible promoter. Renard et al teaches a stable cell line expressing the NMDA receptor subunits under the control of a tetracycline inducible promoter in HEK293 cells (abstract; page 321 right column, fourth paragraph bridging page 323, left column, first paragraph).

Uchino et al do not teach the use of potassium ion channels in an inducible system for drug screening. Grissmer et al teaches screening drugs that modulate potassium ion channels by using a stable cell line that expresses potassium ion channels, contacting the cells with a drug and measuring the potassium ion current

(abstract; page 1230, right column bridging to page 1231, left column, first paragraph and figure 3).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Uchino to use tetracycline to control the expression of a potassium ion channel in a stable cell line for drug screening because Uchino et al teach that it is within the skill of the art to use an inducible promoter to control the expression of an ion channel target in a system to screen drugs and Renard et al and Grissmer et al teach that a tetracycline inducible promoter system can be used to induce the expression of an ion channel target molecule such as a potassium ion channel in drug screening system.

One would have been motivated to do so in order to receive the expected benefit, as suggested by Uchino et al and actually exemplified by Renard et al and Grissmer, of using a system that screens for drugs that modulate potassium ion channels in which the expression of the potassium ion channel is controlled by tetracycline. Absent of any evidence to the contrary, there would have been reasonable expectation of success in using a system of tetracycline controlled expression of a potassium ion channel target in the stable cell to screen for potential drugs since tetracycline has been successfully used as an inducible expression system for many genes and it is known that potassium ion channels are a target of many compounds that can have a therapeutic effect on a cell.

Claims 41-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uchino et al (Molecular Brain Research, 1997, volume 44, pages 1-11) in view of Choi et al (Journal of Neuroscience Methods, 2000, volume 94, pages 217-225).

The teachings of Uchino et al have been described previously. Uchino et al do not teach the conditional expression of a G-protein coupled receptor.

Choi et al teach the inducible expression of the dopamine D2L receptor which is a G-protein coupled receptor in HEL293 cells, measuring the activity of the receptor by cAMP levels and testing the effect of an agonist on the activity of the dopamine D2L receptor (abstract; page 220, left column, second paragraph and right column, second and third paragraphs).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Uchino et al screen for compounds modulating the activity of a G-protein coupled receptor because Uchino et al teach that it is within the skill of the art to express it is within the skill of the art to screen drugs against the activity of a target molecule that is conditionally expressed and because Choi et al teach that the activity dopamine D2L receptor can be monitored in an inducible system for the effects of agonists using cAMP levels. One would have been motivated to do so in order to receive the expected benefit, suggested by Uchino et al and exemplified by Choi et al, of screening compounds that modulate G-protein coupled receptors in an inducible system where the effects of the compounds can be measured by cAMP levels. Absent to any evidence to the contrary, there would have been a reasonable expectation of

success in using G-protein coupled receptor as the target in the drug screening system since the system has been shown to work with similar molecules.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tara L Garvey whose telephone number is (571) 272-2917. The examiner can normally be reached on Monday through Friday 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) (http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the

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Tara L Garvey
Examiner
Art Unit 1636

TLG

JAMES KETTER
PRIMARY EXAMINER